

## TB Suspect Case Presentation and Discussion

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## Diagnosis of Tuberculosis

- Clinical suspicion is the single most important factor in the timely diagnosis of tuberculosis.
- The greatest risk for nosocomial transmission of tuberculosis is exposure to an undiagnosed case of TB.
- There is no diagnostic substitute for thinking about the diagnosis.



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## Good Outcomes Depend on Complete Evaluation and a Correct Diagnosis

- Medical Evaluation
  - Signs and symptoms
  - **History of risk factors and/or exposures**
  - Physical exam
- Chest X-ray
- Bacteriology
  - Cultures of suspected site
  - Susceptibility testing of positive isolate
  - Rapid diagnostic tests (HPLC, NAA)



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## Postprimary (Reactivation) Disease

- “Parenchymal opacities situated in the apical and posterior segments of the upper lobes and the superior segment of the lower lobes, often associated with cavitation, are the characteristic radiographic manifestations of postprimary TB.”



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## Progressive Primary TB: Radiographic Findings

- Parenchymal disease: areas of greatest ventilation-lower and middle lobes
- Lymphadenopathy
- Pleural effusion
- Miliary tuberculosis
- Obstructive atelectasis due to lymphadenopathy
- Normal chest radiograph



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## TB and AIDS: Radiographic Appearance

- The radiographic manifestations of HIV-associated pulmonary TB are dependent on the level of immuno-suppression.
  - Relatively intact cellular immune function (CD4 > 200): radiographic findings similar to non-HIV infected individuals (upper lobe, cavitory disease)
  - Severe immunosuppression (CD4 < 200): findings c/w primary disease or normal chest radiographs or dissemination with miliary pattern or extrapulmonary disease



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## Atypical Presentation of TB

- HIV infection, chronic renal disease, diabetes, immunosuppression may alter presentation
  - CXR may be atypical; lower lobe infiltrate, adenopathy or completely normal
  - Negative TST or QFT Gold
  - Negative smear in up to 50%
  - Atypical clinical presentation



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## Reasons a Diagnosis of TB is Missed or Delayed

- Patient is diagnosed as a community acquired pneumonia and responds to a fluoroquinolone
- Atypical clinical and radiographic picture
- Extrapulmonary disease
- Clinician does not consider TB a diagnosis



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## Delayed TB Diagnosis

- Patient from Mexico in his mid 30's, in the U.S. more than a year, presented to local ED with cough, fever
- Patient treated with oral fluoroquinolone with mild, transient improvement, but symptoms relapsed
- Represented to ED and given FQ again, little symptomatic change
- After 4 months, seen in different ED, sputum sent for AFB which was 4+ AFB positive



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### Delayed TB Diagnosis

- Patient with multiple contacts: family, co-workers, healthcare workers and multiple skin test conversions
- Started on RIPE, *M. tuberculosis* isolate susceptible to first line medications
- Successfully treated with 9 months standard medication

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### Delay in Diagnosis of TB With Empiric Antibiotic Use

- Prospective study to assess delay in diagnosis
  - 85/158 Tb patients received antibiotics for non-TB dx before TB dx
    - 30 patients received more than one course
    - 52 courses FQN to 45 patients (38%)
    - 33 courses macrolides to 29 patients (24%)
    - 11 courses amoxicillin
    - 11 courses cephalosporins
    - 10 courses trimethoprin-sulfamethoxazole
    - 2 courses of clindamycin, 1 of vancomycin
    - 17 courses unknown

» Int J Tuberc Lung Dis 2005;9:392-397

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### Delay in Diagnosis of TB With Empiric Antibiotic Use

- Median delay 39 days compared to 15 controls who did not receive antibiotics
- Delay similar with all antibiotic classes
- 41/54 (79%) patients who did not get CXR at first visit received antibiotics
- 41/105 (42%) with CXR at 1<sup>st</sup> visit received antibiotics
  - 31/54 (57%) dx with CAP received CXR
- More widespread use of CXR may help

HEART Land Int J Tuberc Lung Dis 2005;9:392-397

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### Empirical treatment of community-acquired pneumonia and the development of fluoroquinolone-resistant TB.

Long et al, Clin Infect Dis 2009; 48: 1354-60

- 74/428 patients with TB had received  $\geq 1$  fluoroquinolone (FQ) prescription within 6 months of TB diagnosis
- 3/148 M. tuberculosis isolates FQ resistant: all patients had received multiple FQ prescriptions
- Single FQ prescriptions not associated with FQ resistance, but multiple FQ prescriptions were associate with FQ resistance.

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### Case 1: OE

- 29 yo man from Mexico, in the U.S. 4 years, frequent travel to Florida, Mexico
- One year of symptoms including cough, fever, malaise, weight loss
- Abnormal CXR with cavity treated as community acquired pneumonia on multiple occasions
- Referred to DSHS for enlarging cavity

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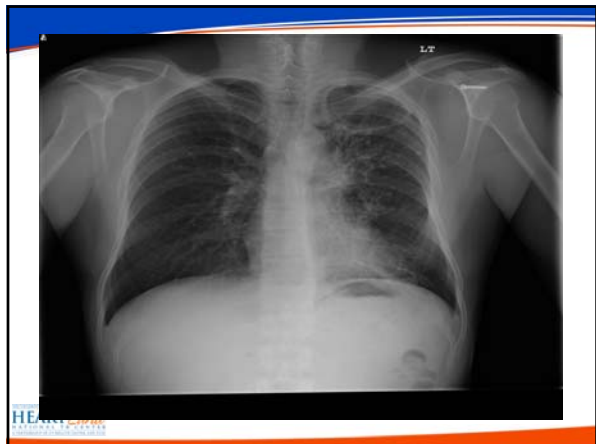
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### Case 1: OE

- 31 contacts tested by DSHS
- Multiple children (family and non-family) cared for in the patient's home
- 21 (+) PPD results
- 6 active cases, all children (ages 1 yr, mos to 10 yrs, 8 mos)



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### Case 2: IM

- 2 yrs 3 mos old female
- Contact to OE
- Asymptomatic



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**Case 4: VM**

- 2 yrs 3 mos male
- Contact to OE
- Asymptomatic

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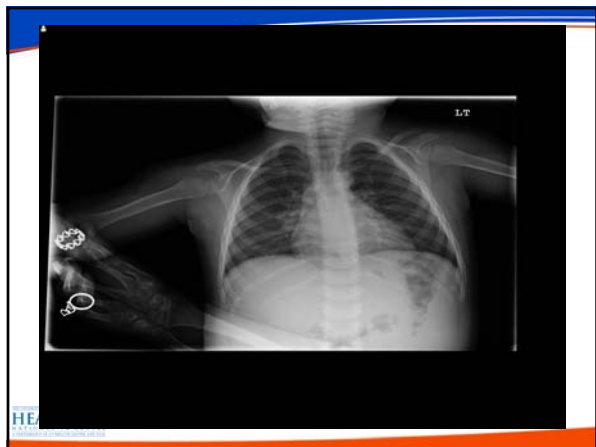
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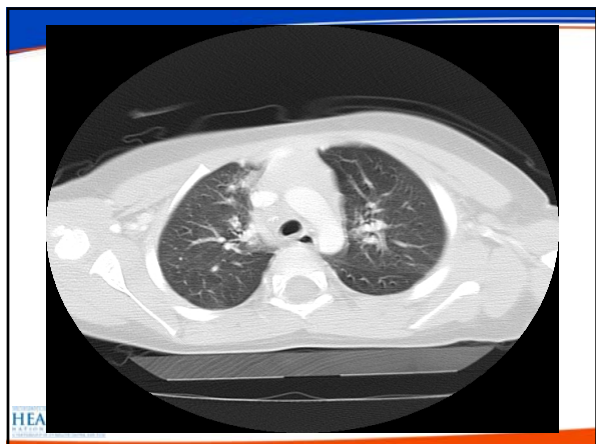
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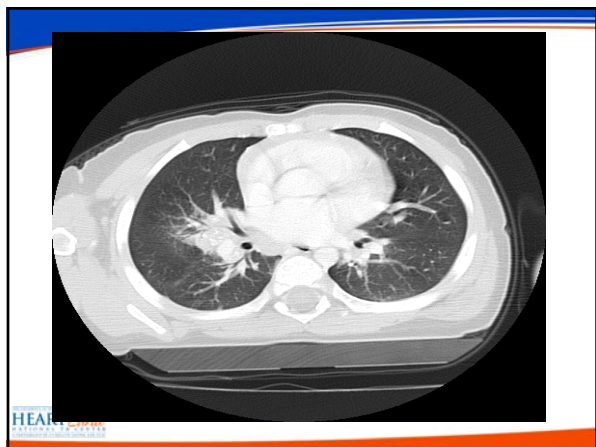
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### Delayed TB Diagnosis

- 25 yr old male with 9 month history of cough and weight loss
- ER visit 6 months earlier for “bronchitis”
- Incarcerated along border x 2 yrs
- Large # family contacts and small children
- Worked as a caterer
- Picked up from mall by EMS due to severe coughing spell

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## CXR in the ER - 6 mo before Dx



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## Delayed Diagnosis of TB

- 32 yo female immigrant from high incident area (FSU), homelessness, incarceration, IVDU, exposure to TB
- prolonged cough, sputum, fever, weight loss, night sweats
- Positive tuberculin skin test (TST) (no therapy)
- Positive QuantiFeron TB Gold Test
- CXR with upper lobe cavitary infiltrates

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TB in a Recent Refugee



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### Delayed TB Diagnosis

- Abnormal chest radiograph, AFB smears and cultures initially negative
- Dental abscess, treated with PCN as aspiration pneumonia
- Several months later, presented with hemoptysis, weight loss
- Sputum AFB smear and culture (+) for INH resistant TB



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### Tuberculosis in the Foreign-born

Risk for drug resistant TB



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### Entering the U.S. with Active TB

- Enter the U.S. as a tourist, for business, as a student or as a temporary worker, etc...
- Enter the U.S. illegally
- A classification on medications
- B1 classification with false negative smears
- B2 classification with false negative CXR
- "Asymptomatic" children, (immuno-compromised adults) with primary TB



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## Delayed TB Diagnosis

- 32 yo man recently entered the U.S. from Ethiopia
- History of 2 episodes of previous TB therapy
- Initial sputum AFB smear negative, QFT TB-gold (+)
- Treated initially for community acquired pneumonia



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## Global Epidemiology of Multidrug Resistant (MDR) TB

- MDR TB: Resistant to INH and Rifampin
- Estimated global prevalence of multidrug (MDR) resistant TB
  - Estimated 500,000 cases
  - Newly diagnosed cases: 2.3%
  - Previously treated cases: 16.4%



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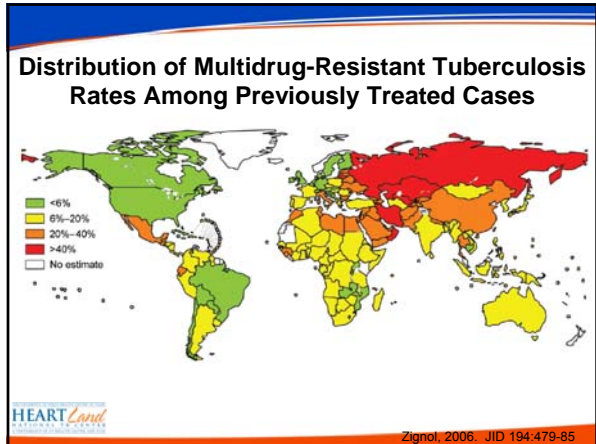
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### Definitions of Drug Resistant Tuberculosis

- MDR TB is the precursor of XDR TB
- XDR TB: MDR TB
  - PLUS
  - Resistance to any fluoroquinolone
  - Resistance to at least one of the following injectables:
    - Amikacin, Kanamycin, Capreomycin

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### Drug Resistant Tuberculosis Creation of XDR TB

- The development of XDR TB results from TB control and treatment practices in most of the world that would not be acceptable in the United States
- Case identification and treatment response are based on AFB smears without confirmatory cultures or susceptibility testing.
- Retreatment for treatment failure not based on in vitro susceptibility studies, rather, on fixed retreatment regimens.

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## Delayed TB Diagnosis

- Patient did not improve with antibacterial therapy
- Repeat sputum AFB smear and culture positive
- *M. tuberculosis* isolate susceptible to all first line antituberculosis drugs (whew!)
- Patient successfully treated



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## Entering the U.S. with Active TB

- Mr. RF, 71 yo man from China
- Entered the U.S. as tourist to visit his children in Houston
- Treated multiple times in China for tuberculosis without success (unknown at time of entry to U.S.)
- Presented for medical evaluation because of cough and shortness of breath



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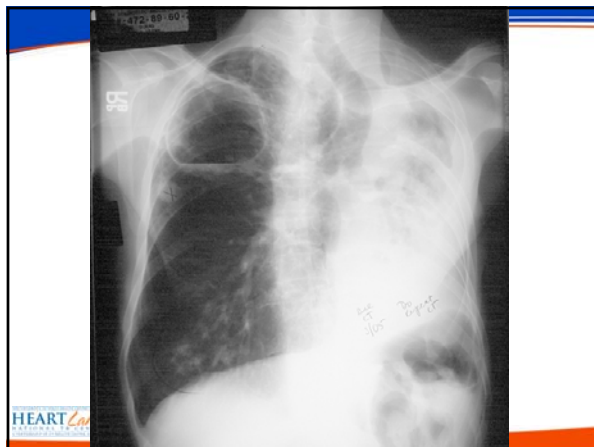
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## Entering the U.S. with Active TB

- RF's sputum 4+ AFB smear pos, culture pos for MTB resistant to: INH, Rif, Rbt, EMB, PZA, STM, AMK, fluoroquinolones
- Treated with Eth, Cap, Cyc, PAS, linezolid
- Within 3 mos, sputum converted to AFB smear and culture negative
- Hospitalized 4 mos, returned to Houston



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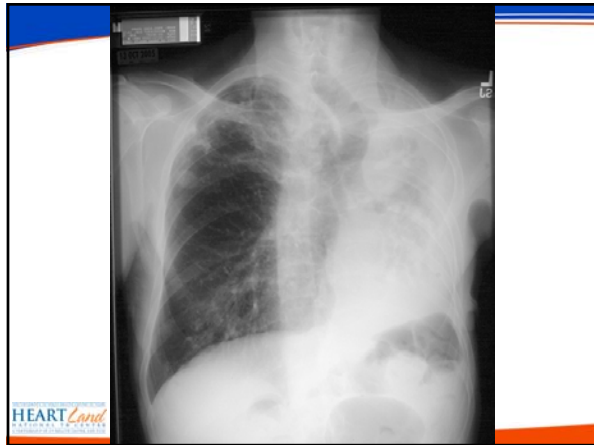
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## Difficult Tuberculosis Diagnosis

Extra-pulmonary TB



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## Fever in 7<sup>th</sup> month of Pregnancy

6 month history of cervical adenopathy  
6 week history of fever, wt loss and abdominal pain  
Tuberculin skin test negative  
No response to multiple antibiotics  
Pleural effusion and infiltrate on CXR



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## Delayed TB Diagnosis

Pulmonary consult for thoracentesis:  
Cervical node biopsy: AFB+, granuloma  
Disseminated disease  
nodes, lung, liver, ascites, multiple abdominal masses, **placenta**, ovaries, bowel  
Clinical deterioration, hypotension, emergent C section



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## Missed Diagnosis

Pulmonologist consulted for thoracentesis  
obtained a **history of risk factors** for TB

Born in Mexico  
Prior +TST at US entry at age 15  
Treated with INH x 6 mo  
Exposure to uncle in Mexico who died with TB 2  
years ago

***TST usually negative with extensive disease!***



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## Delayed TB Diagnosis

M Tb resistant to INH grew from sputum and  
nodes

Infant also treated for tuberculosis as  
placenta was positive for AFB

Mother and child recovered from TB



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## Guidelines for Evaluation of Pulmonary TB in Adults

- Any cough  $\geq$  2-3 wks plus at least **one** additional symptom: fever, night sweats, weight loss or hemoptysis
- Any high risk for TB; unexplained illness including respiratory symptoms  $\geq$  2-3 wks
- CXR: if suggestive of TB collect 3 sputum specimens for AFB and culture
- CXR: if suggestive of TB collect 3 sputum specimens for AFB and culture



Controlling TB in U.S. MMWR: Nov 2005

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## Guidelines for Evaluation of Pulmonary TB in Adults

- Any HIV infected with unexplained cough and fever
- Any at high risk for TB with dx CAP & not improved >7days
- Any at high risk for TB with incidental findings on CXR of TB even minimal/no sx
- CXR and collect 3 sputum for AFB smear and culture
- CXR and 3 sputum for AFB smear and culture
- Review prior CXR if available, 3 sputum for AFB smear and culture



Controlling TB in U.S. MMWR: Nov 2005

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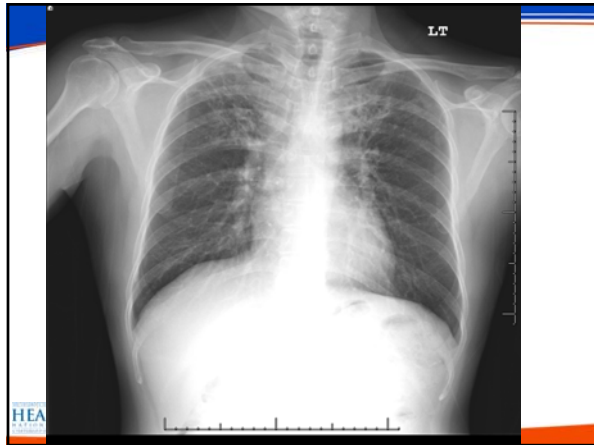
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